Abstract

Human α_2-antiplasmin (α_2AP) is the major inhibitor of the proteolytic enzyme plasmin that digests fibrin. Two forms of α_2AP circulate in human plasma: a 464-residue protein, which we have termed "pro"-form, or $\alpha_2AP_{pro,}$ and an N-terminally-shortened 452-residue "activated"-form, or α_2AP_{act}. The latter becomes crosslinked to fibrin by activated factor XIII about 5-fold more rapidly than α_2AP_{pro} and makes fibrin resistant to digestion by plasmin. A new human plasma proteinase has been identified herein that cleaves the Pro12-Asn13 bond of α_2AP_{pro} to yield α_2AP_{act}. This enzyme is identified herein as Antiplasmin Cleaving Enzyme (APCE).

Novel inhibitors of circulating APCE can diminish α_2AP inhibitory capacity within forming fibrin or blood clots thereby making fibrin deposits or blood clots more susceptible to removal by plasmin. Patients who are susceptible to atherosclerotic plaque formation or are susceptible to developing thrombi that compromise organ function will benefit by therapies providing such inhibitors on a long term basis.